

LAID-OPEN PATENT GAZETTE, JAPANESE PATENT OFFICE (JP)(A)

Laid-Open Number: 2000/327,557

Laid-Open Date: 28 November 2000

Application Number: 11/143,152

Application Date: 24 May 1999

Int. Cl.⁷: A 61 K 7/48, 7/00, 31/00, 47/32
// B 01 F 17/42, 17/52, B 01 J 13/00

Inventors: Yoshihito Seto, Yasuhiro Fukuda,
Masahiro Torihara and Yoshin Tamai
Applicants: Pola Chemical Industry Co., Ltd.
6-48 Yayoicho, Shizuoka-shi, Shizuoka-ken
and
Kuraray Co., Ltd.
1621 Sakatsu, Kurashiki-shi, Okayama-ken
Representatives: Tsutomu Toyama, Patent Attorney
and two more

EMULSIFIED COMPOSITION

Abstract:

[Matters to Solve]

An object of the present invention is to provide an emulsified composition such as a cosmetic and a medicament for external application to the skin containing a resorcinol derivative such as 4-n-butylresorcinol, wherein the pharmaceutical effect of the resorcinol derivative is enhanced and, at the same time, sufficient safety and stability of the preparation are ensured.

[Solving Means]

An emulsified composition is compounded with an unsaturated higher alcohol ether of polyhydric alcohol such as glycerol, 4-n-butylresorcinol represented by the following formula (I) and/or salt thereof and, preferably, a high-molecular substance having an alkyl group such as an alkyl methacrylate/acrylic acid copolymer and/or salt thereof.



What is Claimed is:

1. An emulsified composition which is characterized in containing an unsaturated higher alcohol ether of polyhydric alcohol and a resorcinol derivative.
2. The emulsified composition according to claim 1, wherein the polyhydric alcohol is glycerol or diethylene glycol.
3. The emulsified composition according to claim 1 or 2, wherein the unsaturated higher alcohol is oleyl alcohol.
4. The emulsified composition according to any of claims 1 to 3, wherein the resorcinol derivative is 4-n-butylresorcinol represented by the formula (I) and/or a salt thereof.



5. The emulsified composition according to any of claims 1 to 4, wherein a high-molecular substance having an alkyl group is further contained therein.
6. The emulsified composition according to any of claims 1 to 5, wherein the high-molecular substance having an alkyl group is an alkyl methacrylate/acrylic acid copolymer and/or a salt thereof.
7. The emulsified composition according to any of claims 1 to 6, wherein the composition does not contain a nonionic surface-active agent.
8. The emulsified composition according to any of claims 1 to 7, wherein the composition is a cosmetic.

Detailed Description of the Invention:

[0001]

[Technical Field to which the Invention Belongs]

The present invention relates to an emulsified composition containing a resorcinol derivative and, more particularly, it relates to an emulsified composition having sufficient safety and stability of the preparation and, at the same time, the pharmaceutical effect of the resorcinol derivative is enhanced.

[0002]

[Prior Art]

A resorcinol derivative has an inhibitory action for the production of melanin and an antibacterial action and also has a good stability whereby it is useful as an effective ingredient for an agent for external application to the skin such as a cosmetic and a medicament for external application to the skin. Therefore, in order to enhance such an action of the resorcinol derivative, there has been a demand for its appropriate preparation. Thus, skin is a protective wall for shielding the organism from the outer world whereby permeation of chemical substances, etc. is significantly suppressed by the skin and there has been a demand for a preparation where the permeation of the above-mentioned resorcinol derivatives is enhanced. However, when permeation of chemical substances such as the resorcinol derivative is merely enhanced, it sometimes happens that percutaneous absorption of nonionic surface-active agent, etc. used for the stabilization for the system is also enhanced and, since that may results in irritation or the like, there has been also demanded a countermeasure for avoiding such an undesired phenomenon. There has been a particular demand for developing a preparation which contains no nonionic surface-active agent and still has a sufficient stability. Especially in a form of milky lotion having a low viscosity (not higher than 8,000 c.s. under the condition of 5°C), a form design for making the system stable without compounding of nonionic surface-active agent, etc. is difficult and there has been a demand for an art of conducting such a form design.

[0003]

On the other hand, ether of polyhydric alcohol with higher alcohol has been used in emulsified compositions such as cosmetics with an object of supplementing the stabilization of the system or improving the feel. However, it has been unknown that the effect of resorcinol derivative is enhanced by the joint use of the resorcinol derivative with the above-mentioned higher alcohol ether of polyhydric alcohol and also that such a joint use is able to be used in an emulsified system where nonionic surface-active agent is absent. It has been also unknown at all that such a higher alcohol ether of polyhydric alcohol is contained in an emulsified composition together with a high-molecular substance having an alkyl group and further that the emulsified product as such has good stability and physical property. It has been further unknown that, in many cases, viscosity of such a stable emulsified composition is not so high.

[0004]

[Problem that the Invention is to Solve]

The present invention has been conducted under such circumstances and an object of the present invention is to provide an emulsified composition such as a cosmetic and a medicament for external application to the skin containing a resorcinol derivative such as 4-n-butylresorcinol, wherein the pharmaceutical effect of the resorcinol derivative is enhanced and, at the same time, sufficient safety and stability of the preparation are ensured.

[0005]

[Means for Solving the Problem]

In order to solve the above-mentioned problem, the present inventors have carried out intensive studies and investigations for seeking a preparation in an emulsified composition containing the resorcinol derivative such as cosmetics and medicaments for external application to the skin where pharmaceutical effect of the resorcinol derivative is enhanced, risk of percutaneous absorption of surface-active agent and the like is not resulted, sufficient stability is available and, preferably, nonionic surface-active agent is not contained. As a result, it has been found that an emulsified composition having the above-mentioned characteristics being compounded

with the resorcinol derivative when an emulsified composition is compounded with an unsaturated higher alcohol ether of polyhydric alcohol and, preferably, a high-molecular substance having an alkyl group together with the resorcinol derivative whereupon the present invention has been achieved.

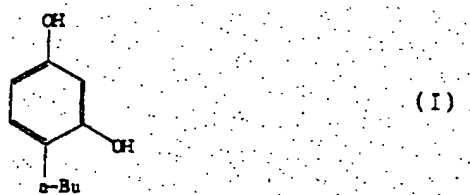
[0006]

Thus, the present invention is an emulsified composition which is characterized in containing an unsaturated higher alcohol ether of polyhydric alcohol and a resorcinol derivatives. With regard to the polyhydric alcohol in the unsaturated higher alcohol ether of polyhydric alcohol used in the emulsified composition of the present invention, glycerol and diethylene glycol are preferably exemplified while, with regard to the unsaturated higher alcohol therein, oleyl alcohol is preferably exemplified.

[0007]

With regard to the resorcinol derivative contained in the emulsified composition of the present invention, 4-n-butylresorcinol represented by the formula (I) and/or a salt thereof are/is exemplified.

[0008]



[0009]

In the emulsified composition of the present invention, it is preferred to contain a high-molecular substance having an alkyl group in addition to the above-mentioned unsaturated higher alcohol ether of polyhydric alcohol and the resorcinol derivative. With regard to the said high-molecular substance having an alkyl group, an alkyl methacrylate/acrylic acid copolymer and/or a salt thereof are/is exemplified.

[0010]

With regard to the emulsified composition of the present invention, that which is prepared without compounding a nonionic surface-active agent is preferred. Further, the emulsified composition of the present invention is preferably used as a cosmetic.

[0011]

[Embodiments of the Invention]

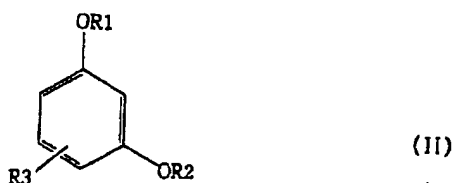
As hereunder, embodiments of the present invention will be illustrated.

[0012]

(1) The resorcinol derivative which is an essential component of the emulsified composition of the present invention

In the emulsified composition of the present invention, the resorcinol derivative is an essential component. The resorcinol derivative used in the present invention means a 1,3-dihydroxyphenol derivative represented by the following formula (II) and/or a physiologically acceptable salt thereof.

[0013]



[0014]

(In the formula, R_1 and R_2 each independently is hydrogen atom, an acyl group having 1~4 carbon(s), an alkyl group having 1~4 carbon(s), mesyl group or tosyl group; and R_3 is an alkyl group or hydrogen atom.)

[0015]

With regard to the above-mentioned resorcinol derivative used in the present invention, an alkylresorcinol of the formula (II) where both R_1 and R_2 are hydrogen atom and R_3 is an alkyl group and/or a physiologically acceptable

salt thereof are/is preferably exemplified. With regard to the said alkyl group, an alkyl group containing a linear, branched or cyclic structure having about 4 to 7 carbons is preferably exemplified and n-butyl group is more preferably exemplified. With regard to the bonding site of the said alkyl group, 2- or 4-position is preferred. Thus, with regard to the said alkyl group, n-butyl group bonded to 2- or 4-position is preferred and that bonded to 4-position is particularly preferred. Thus, among the resorcinol derivatives used in the present invention, 4-n-butylresorcinol having the structure of the above-mentioned formula (I) and/or salt thereof are/is particularly preferred.

[0016]

Among the resorcinol derivative used in the present invention, the 1,3-dihydroxyphenol derivative represented by the formula (II) may be prepared by the conventional method where resorcinol is used as a starting substance and hydrogens of hydroxyl groups bonded to 1- and 3-carbons or hydrogens bonded to carbons at 1- and 3-positions are substituted with acyl group, alkyl group, mesyl group, tosyl group, etc. Method for the manufacture of the alkylresorcinol which is advantageously used in the present invention among those derivatives is mentioned, for example, in Japanese Patent Laid-Open No. 02/49,715, etc. and it is also possible to refer thereto. Thus, the alkylresorcinol may be easily prepared by a method where resorcinol is fused with a saturated carboxylic acid in the presence of zinc chloride and the resulting condensate is reduced with amalgam/hydrochloric acid (refer to Lille, J., Bitter L. A., Peiner, V., Tr. Nauch - Iasled. Inst. slantsev, 1969, No. 18, 127) or by a method where resorcinol is made to react with the corresponding alkyl alcohol using an alumina catalyst at the temperature of as high as 200~400°C (refer, for example, to British Patent No. 1,581,428), etc.

[0017]

With regard to a salt, there will be no particular limitation so far as it is physiologically acceptable and its appropriate examples are alkaline metal salt such as sodium salt and potassium salt; alkaline earth metal salt such as calcium salt and magnesium salt; organic amine salt such as ammonium salt, triethanolamine salt and triethylamine salt; and basic amino acid salt such as lysine salt and arginine salt. Among the above, particularly preferred one is an alkaline metal salt and, among those, especially

preferred one is a potassium salt.

[0018]

The above-mentioned resorcinol derivative used in the present invention has a physiologically active action such as an action for the suppression of production of melanin and an antibacterial action. In the emulsified composition of the present invention, the preferred amount of the said resorcinol derivative for achieving the above-mentioned physiologically active action and for manufacturing a preparation is 0.01~10% by weight or, more preferably, 0.05~5% by weight to the total amount of the composition.

[0019]

(2) Unsaturated higher alcohol ether of polyhydric alcohol which is an essential component of the emulsified composition of the present invention

The emulsified composition of the present invention contains unsaturated higher alcohol ether of polyhydric alcohol as an essential component. With regard to the polyhydric alcohol which is able to be used for constituting the said ether, there is preferably exemplified a polyhydric alcohol having 2 to 5 carbons. Specific and preferred examples of such a polyhydric alcohol are ethylene glycol, glycerol, pentyl glycol, neopentyl glycol, erythritol, diethylene glycol, propylene glycol, 1,3-butanediol and dipropylene glycol. More preferred examples are glycerol and diethylene glycol and glycerol is particularly preferred.

[0020]

With regard to unsaturated higher alcohol which is another element for constituting the said ether, that having 4 to 24 carbons is preferred and that having 12 to 24 carbons is more preferred. Its specific and preferred examples are butenol, pentenol, propargyl alcohol, octenol, decenol, dodecenol and oleyl alcohol and, among those, oleyl alcohol is particularly preferred.

[0021]

In the polyhydric alcohol, all hydroxyl groups in the same molecule may be etherized or a part of them may be etherized. Preferred one is that where

hydroxyl group(s) remain(s) in a molecule. Accordingly, examples of the preferred ether are ethylene glycol monooleyl ether, diethylene glycol monooleyl ether, glycerol- α -monooleyl ether, glycerol- β -monooleyl ether, glycerol- α,β -dioleylether, glycerol- α,α -dioleylether and neopentyl glycol monooleyl ether. Among those, more preferred examples are diethylene glycol monooleyl ether, glycerol- α -monooleyl ether, glycerol- β -monooleyl ether, glycerol- α,β -dioleylether and glycerol- α,α -dioleylether and particularly preferred ones are glycerol- α -monooleyl ether and glycerol- β -monooleyl ether.

[0022]

In the present invention, such an unsaturated higher alcohol ether of polyhydric alcohol is contained in the emulsified composition together with the above-mentioned resorcinol derivative whereby enhancement of effect of the resorcinol derivative is possible. The said unsaturated higher alcohol ether of the polyhydric alcohol has not only an action of enhancing the effect of the resorcinol derivative but also has an action of stabilizing the system of the emulsified composition.

[0023]

The preferred amount of the said ether in the emulsified composition of the present invention is 0.01~5% by weight or, more preferably, 0.1~3% by weight to the total amount of the emulsified composition. The reason why the above-mentioned range is preferred for the amount of the ether is that, when the amount is too much, viscosity of the system of the emulsified composition may sometimes become high while, when it is too small, an effect of stabilizing the system may not be sometimes available.

[0024]

(3) High-molecular substance having an alkyl group which is a preferred optional component for the emulsified composition of the present invention

The emulsified composition of the present invention contains a high-molecular substance having an alkyl group as a preferred optional component. When an emulsification is carried out using the said high-molecular substance in combination with the above-mentioned resorcinol derivative and unsaturated higher alcohol ether of polyhydric

alcohol, it is possible to suppress the detachment of a cosmetic and to make the acting time longer. In addition, as a result of the use of the said high-molecular substance, it is also possible to enhance the physiologically active action of the resorcinol derivative.

[0025]

With regard to the high-molecular substance having an alkyl group used in the present invention, preferred examples are polymers and/or copolymers where the constituting monomer(s) is/are one or more which is/are selected from acrylic acid and alkyl ester or alkylamide thereof, methacrylic acid and alkyl ester or alkylamide thereof, acylated vinyl alcohol and alkyl ether thereof, styrene and α -alkylstyrene. Further examples of the high-molecular substance having an alkyl group used in the present invention are physiologically acceptable salts of the above-mentioned polymers and copolymers. Among those, preferred example(s) of the high-molecular substance having an alkyl group used in the present invention is/are alkyl methacrylate/acrylic acid copolymer and/or salt thereof.

[0026]

With regard to the alkyl group in the high-molecular substance having an alkyl group, it is preferred to be a long-chain alkyl. To be more specific, an alkyl group having 8~34 carbons is preferred and that having 10~32 carbons is more preferred. The high-molecular substance having an alkyl group used in the present invention may be manufactured, for example, by such a method that one or more monomer(s) selected from the above-exemplified ones is/are used as material(s) and polymerized by the same method as in the conventional polymerization of the monomer(s) selected as such. To be more specific, in the case of the manufacture of the alkyl methacrylate/acrylic acid copolymer which is preferably used in the present invention, methacrylic acid, methacrylic acid is converted to a chloride using thionyl chloride or the like and made to react with alcohol or alkylamine in the presence of an alkali and the resulting alkyl methacrylate is copolymerized with acrylic acid.

[0027]

Many of the above-mentioned high-molecular substance used in the present

invention have been already available in the market and it is possible to use them in the present invention. Preferred examples of such commercially available products are alkyl methacrylate/acrylic acid copolymers (carbon number of the alkyl group: 10~30) and/or salts thereof sold from Goodrich under the trade names of Pemrene TR-2 and Pemrene TR-2.

[0028]

With regard to the salt mentioned here, any salt may be used so far as it is physiologically acceptable and its preferred examples are alkaline metal salt such as sodium salt and potassium salt; alkaline earth metal salt such as calcium salt and magnesium salt; organic amine salt such as ammonium salt, triethylamine salt and triethanolamine salt; and basic amino acid salt such as lysine salt and arginine salt. Among those, the most preferred one is an alkaline metal salt.

[0029]

The preferred amount of such a high-molecular substance having an alkyl group in the emulsified composition of the present invention is 0.01~2% by weight and, more preferably, 0.05~1% by weight. The reason why the above-mentioned range is preferred for the amount of the high-molecular substance having an alkyl group is that, when the amount is too much, the product may become too thick while, when it is too small, a stabilizing action may not be achieved.

[0030]

(4) Emulsified composition of the present invention

The emulsified composition of the present invention is characterized in containing the above-mentioned resorcinol derivative and unsaturated higher alcohol ether of polyhydric alcohol and, preferably, in further containing a high-molecular substance having an alkyl group. When the emulsified composition is made in the composition as such in accordance with the present invention, a physiologically active action of the resorcinol is enhanced and, in addition, there is no risk of an excessive percutaneous absorption of components which are not preferred to be absorbed such as surface-active agent. Thus, it is now possible to manufacture an emulsified preparation which is safe and has a sufficient stability.

[0031]

Application of the emulsified composition of the present invention is not particularly limited but the composition is applicable to any composition so far as it is an emulsified system. To be more specific, it is applied to the fields of cosmetics and medicaments for external use such as to the skin in a form of milky lotion, cream, etc. although the preferred field to which the present invention is applied is cosmetics.

[0032]

In addition to the above-mentioned essential components, i.e. the resorcinol derivative and the unsaturated higher alcohol ether of polyhydric alcohol and the above-mentioned preferred optional component, i.e. the high-molecular substance having an alkyl group, the emulsified composition of the present invention may also contain substrate components which are commonly used in emulsified compositions in the field where the emulsified composition of the present invention is applied such as cosmetics and medicaments for external use such as to the skin or, in other words, components such as aqueous component, oily component and emulsifier which are necessary for the formation of an emulsified composition in combination with the already-mentioned components. Type and composition of the substrate component necessary for the formation of the emulsified composition are appropriately selected depending upon the use and the emulsion form and such an appropriate selection has been commonly carried out by persons skilled in the art.

[0033]

Examples of the substrate component are water, etc. as the aqueous component while, as the oily component, they are hydrocarbon such as Vaseline and microcrystalline wax; ester such as jojoba oil and whale wax; triglyceride such as beef tallow and olive oil; higher alcohol such as cetanol and oleyl alcohol; fatty acid such as stearic acid and oleic acid; and polyhydric alcohol such as glycerol and 3-butanediol. With regard to the emulsifier, various kinds of surface-active agents may be used.

[0034]

When the emulsified composition of the present invention is a medicament for external application to the skin, it usually contains effective ingredients such as antifungal agent, anti-inflammatory agent, steroid, anti-itching agent and antibiotic substance. Besides the above-mentioned components, it is also possible to use optional components which are commonly compounded in cosmetics and medicaments for external application to the skin such as ethanol, thickener such as Carbopol, antiseptic agent, ultraviolet absorber, antioxidant, dye, powder, etc. and also various pharmaceutical ingredients. Such optional components may be compounded within such an extent that the advantage of the present invention is not deteriorated.

[0035]

The emulsified composition of the present invention can be manufactured by treating those components by means of a conventional method. Although the emulsified composition of the present invention is able to contain a nonionic surface-active agent as an optional component as mentioned above, it is also possible to apply the present invention to an emulsified system containing no nonionic surface-active agent and, in view of safety, an emulsified composition containing no nonionic surface-active agent is preferred. Especially when the emulsified composition of the present invention contains the high-molecular substance containing an alkyl group, an emulsified system having a good stability can be formed even in the absence of the nonionic surface-active agent. Accordingly, it is particularly preferred that the emulsified composition is prepared using the high-molecular substance in addition to the above-mentioned resorcinol derivative and unsaturated higher alcohol ether of polyhydric alcohol without the use of nonionic surface-active agent.

[0036]

In the emulsified system which has been commonly known, there is a tendency that viscosity of the emulsified preparation having a high safety becomes high whereby the spread in actual use becomes heavy. However, according to the emulsified composition of the present invention where the high-molecular substance having an alkyl group is contained, it is possible to manufacture a preparation having both safety and stability even under the viscosity of as low as not higher than 8,000 c.s. (under the condition of 5°C) whereby an emulsified composition having a good spread and good usability

is prepared. A specific example of the emulsified composition having a low viscosity of not higher than 8,000 c.s. (at 5°C) and also having both good safety and stability according to the present invention is that which contains about 1~10% by weight of oily component and about 90~99% by weight of aqueous component to the total amount of the composition and also contains the above-mentioned preferred amounts of the resorcinol derivative, the unsaturated higher alcohol ether of polyhydric alcohol and the high-molecular substance having an alkyl group.

[00037]

[Examples]

The present invention will now be illustrated in more detail by way of the following Examples although it goes without saying that the present invention is not limited to such Examples only.

[0038]

<Example 1>

A cosmetic 1 (cream) which is an emulsified composition of the present invention was prepared according to the formulation shown in the following Table 1. Thus, each of the components (a), (b), (c) and (d) was heated at 80°C, the component (b) was added to the component (a), the mixture was kneaded, the component (c) was added to dilute, emulsification was carried out by adding the component (d) gradually thereto and the mixture was stirred with cooling to prepare a cream.

[0039]

Similarly were manufactured a cream of Comparative Example 1 where glycerol- α -monooleyl ether of the cosmetic 1 was substituted with glycerol- α -monostearyl ether and a cream of Control Example 1 where it was substituted with water and the whitening effects of them and of the above cosmetic 1 were checked.

[0040]

Thus, 4 sites of human forearm (2 cm \times 2 cm) were irradiated with

ultraviolet ray (light source: SE Lamp manufactured by Toshiba) which was 0.5-fold of MED (minimal erythema dose) previously measured in a frequency of once daily for 3 days to prepare a turning model. One of the four turned models as such was applied with the cosmetic 1 of the present invention, another thereof was applied with the cosmetic of Comparative Example 1 and still another thereof was applied with a cosmetic of Control Example 1 in an amount of 0.01 ml/day for three weeks each while the residual one site was not applied with any of them at all (non-treated). Then degree of coloration was observed after 24 hours from the last application and the whitening effect in each site as compared with the degree of coloration of the non-treated site was evaluated according to the standard mentioned as follows. Thus, ++ for very white; + for clearly white; ± for slightly white; and - for not white.

[0041]

The result was that the creams of Control Example 1 and Comparative Example 1 were ± while the cosmetic 1 of the present invention was from + to ++. Accordingly, it is apparent that the cosmetic of the present invention containing the resorcinol derivative together with the unsaturated higher alcohol ether of polyhydric alcohol has better pharmaceutical effect of the resorcinol derivative as compared with Control Example and Comparative Example containing the same amount of the resorcinol derivative.

[0042]

Table 1

Components	Compounding Amount
Component (a)	
70% aqueous solution of maltitose	5 parts by weight
Glycerol	5 parts by weight
1,3-Butanediol	5 parts by weight
4-n-Butylresorcinol	0.1 part by weight
Component (b)	
Glycerol- α -monooleyl ether	1 part by weight
Diglycerol trioleate	5 parts by weight
Methyl paraben	0.3 part by weight
Butyl paraben	0.1 part by weight

Component (c)	
Liquid paraffin	10 parts by weight
Light isoparaffin	20 parts by weight
Component (d)	
Disodium hydrogen phosphate	0.2 part by weight
Water	48.3 parts by weight

[0043]

<Example 2>

A cosmetic 2 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the following Table 2. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 1 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 2 where glycerol- α -monooleyl ether was substituted with glycerol- α -stearyl ether, it was separated within 24 hours after being emulsified at room temperature.

[0044]

After emulsifying the cosmetic 2, it was allowed to stand at room temperature for 24 hours, charged in a preserving bottle and preserved for 24 hours under the following temperature conditions and viscosities measured were as follows. Thus, 4820 at 5°C, 2800 at 20°C and 2000 at 40°C (unit: c. s.). Further, the cosmetic 2 was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner. Furthermore, when the cosmetic 2 was evaluated in terms of the whitening effect by the evaluation method as mentioned above, the result was ++ whereby it was ascertained that the pharmaceutical effect of the

resorcinol was enhanced by the use of an emulsified system where the high-molecular substance having an alkyl group was compounded in addition to the resorcinol derivative and the unsaturated higher alcohol ether of polyhydric alcohol.

[0045]

Table 2

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Glycerol- α -monooleyl ether	0.3 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresocinol	0.1 part by weight
Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-2)	0.2 part by weight
Potassium hydroxide	0.1 part by weight
Maltotriose	0.2 part by weight
Water	87.3 parts by weight

[0046]

<Example 3>

A cosmetic 3 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the following Table 3. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 2 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 3 where glycerol- α -monooleyl ether was substituted with glycerol- α -stearyl ether, it

was separated within 24 hours after being emulsified at room temperature.

[0047]

After emulsifying the cosmetic 3, it was allowed to stand at room temperature for 24 hours, charged in a preserving bottle and preserved for 24 hours under the following temperature conditions and viscosities measured were as follows. Thus, 4800 at 5°C, 2910 at 20°C and 2000 at 40°C (unit: c. s.). Further, the cosmetic 3 was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner.

[0048]

Table 3

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Glycerol- α -monooleyl ether	0.5 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresocinol	0.5 part by weight
Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-2)	0.2 part by weight
Potassium hydroxide	0.1 part by weight
Maltotriose	0.2 part by weight
Water	87.3 parts by weight

[0049]

<Example 4>

A cosmetic 4 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the following Table 4. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 3 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 4 where glycerol- α -monooleyl ether was substituted with glycerol- α -stearyl ether, it was separated within 24 hours after being emulsified at room temperature.

[0050]

After emulsifying the cosmetic 4, it was allowed to stand at room temperature for 24 hours, charged in a preserving bottle and preserved for 24 hours under the following temperature condition and viscosity measured was as follows. Thus, 1960 at 20°C (unit: c. s.). Further, the cosmetic 4 was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner.

[0051]

Table 4

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Glycerol- α -monooleyl ether	0.5 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresocinol	1 part by weight

Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-2)	0.15 part by weight
Potassium hydroxide	0.05 part by weight
Maltotriose	0.2 part by weight
Water	86.3 parts by weight

[0052]

<Example 5>

A cosmetic 5 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the following Table 5. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 4 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 5 where glycerol- α -monooleyl ether was substituted with glycerol- α -stearyl ether, it was separated within 24 hours after being emulsified at room temperature.

[0053]

The cosmetic 5 prepared hereinabove was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner.

[0054]

Table 5

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Glycerol- α -monooleyl ether	0.3 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresocinol	0.1 part by weight
Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-1)	0.2 part by weight
Potassium hydroxide	0.1 part by weight
Maltotriose	0.2 part by weight
Water	87.4 parts by weight

[0055]

<Example 6>

A cosmetic 6 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the following Table 6. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 5 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 6 where glycerol- β -monooleyl ether was substituted with glycerol- α -stearyl ether, it was separated within 24 hours after being emulsified at room temperature.

[0056]

The cosmetic 6 prepared hereinabove was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained

that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner.

[0057]

Table 6

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Glycerol- β -monooleyl ether	0.3 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresocinol	0.1 part by weight
Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-2)	0.2 part by weight
Potassium hydroxide	0.1 part by weight
Maltotriose	0.2 part by weight
Water	87.4 parts by weight

[0058]

<Example 7>

A cosmetic 7 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the following Table 7. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 6 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 7 where

glycerol- β -monooleyl ether was substituted with glycerol- α -stearyl ether, it was separated within 24 hours after being emulsified at room temperature.

[0059]

The cosmetic 7 prepared hereinabove was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner.

[0060]

Table 7

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Glycerol- β -monooleyl ether	0.3 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresocinol	0.1 part by weight
Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-2)	0.2 part by weight
Potassium hydroxide	0.1 part by weight
Maltotriose	0.2 part by weight
Water	87.4 parts by weight

(Translator's comment: Formulation of Table 7 is entirely as same as that of Table 6.)

[0061]

<Example 8>

A cosmetic 8 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the

following Table 8. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 7 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 8 where glycerol- α,β -dioleylether was substituted with glycerol- α -stearyl ether, it was separated within 24 hours after being emulsified at room temperature.

[0062]

The cosmetic 8 prepared hereinabove was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner.

[0063]

Table 8

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Glycerol- α,β -dioleylether	0.3 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresorcinol	0.1 part by weight
Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-2)	0.2 part by weight
Potassium hydroxide	0.1 part by weight
Maltotriose	0.2 part by weight
Water	87.3 parts by weight

[0064]

<Example 9>

A cosmetic 9 (milky lotion) which is an emulsified composition of the present invention was manufactured according to the formulation as shown in the following Table 9. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. In the meanwhile, manufacture of an emulsion was tried where Pemrene TR-2 was substituted with carboxyvinyl polymer as Referential Example 8 but emulsification was not possible. Further, in the case of an emulsion of Comparative Example 9 where diethylene glycol monooleyl ether was substituted with glycerol- α -stearyl ether, it was separated within 24 hours after being emulsified at room temperature.

[0065]

The cosmetic 9 prepared hereinabove was stable even when preserved for 10 days under the condition of as severe as 50°C. It is therefore ascertained that, when the unsaturated higher alcohol ether of polyhydric alcohol the high-molecular substance having an alkyl group are jointly used in the emulsified composition of the present invention containing the resorcinol derivative, an emulsified composition containing no nonionic surface-active agent and having a low viscosity can be prepared in a stable manner.

[0066]

Table 9

Components	Compounding Amount
Component (a)	
Jojoba alcohol	0.5 part by weight
Cetanol	0.5 part by weight
Diethylene glycol monooleyl ether	0.3 part by weight
Jojoba oil	1.7 parts by weight
Methyl phenyl polysiloxane	1 part by weight
Butyl paraben	0.1 part by weight
4-n-Butylresocinol	0.1 part by weight

Component (b)	
1,3-Butanediol	8 parts by weight
Alkyl methacrylate/acrylic acid copolymer (Pemrene TR-2)	0.2 part by weight
Potassium hydroxide	0.1 part by weight
Maltotriose	0.2 part by weight
Water	87.3 parts by weight

[0067]

<Example 10>

Usability of the cosmetics prepared in the above Examples 2 to 9 at 5°C was checked by professional panelists. Usability was checked for the items of good spread, close adhesion feel and good compatibility to skin according to the evaluation standards that where ++ is very good, + is good; ± is a bit good; and – is bad. The result is shown in Table 10. It is noted therefrom that the cosmetics of the present invention have a low viscosity even at low temperature whereby the usability is very good.

[0068]

Table 10

Sample Used	Good Spread	Close Adhesion Feel	Good Compatibility to the Skin
Cosmetic 2	++	++	++
Cosmetic 3	++	++	++
Cosmetic 4	++	++	++
Cosmetic 5	++	++	++
Cosmetic 6	++	++	++
Cosmetic 7	++	++	++
Cosmetic 8	++	++	++
Cosmetic 9	++	++	++

[0069]

<Example 11>

Safety of the cosmetics which were prepared in the above Examples 2 to 9

was checked using skin-injured models of guinea pigs (5 in one group). Hair on the back of the guinea pigs was shaved, a rubber tape stripping was conducted and a close patch test was carried out for 48 hours using the above cosmetics 2 to 9. After removal of the patch, the skin reaction was evaluated by the so-called standard by Draze as shown below. Thus, ++ is reaction accompanied by edema; + is reaction accompanied by apparent erythema; ± is reaction accompanied by slight erythema; and - is no reaction. The result was "no reaction" (-) in all cases where the cosmetics were subjected to a closed patch whereby the high safety of the cosmetics of the present invention was ascertained.

[0070]

<Example 12>

A medicament 1 (milky lotion) for external application to the skin which was an emulsified composition of the present invention for anti-inflammation was manufactured according to the formulation as shown in the following Table 11. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition. The resulting medicament 1 for external application to the skin showed a very good spread and gave little detachment from the skin whereby it was noted that a good substrate material for external application to the skin was used.

[0071]

When the above medicament 1 for external application to the skin was administered to the damaged skin where an anti-inflammatory agent was used, a non-preferred physical irritation by application to the damaged skin in the use of anti-inflammatory agent was suppressed. In addition, as a result of the antibacterial action of the resorcinol derivative, the said medicament 1 for external application to the skin was stable to microbes.

[0072]

Table 11

(a)	Jojoba alcohol	0.5 part by weight
	Cetanol	0.5 part by weight
	Glycerol α -monooleyl ether	0.3 part by weight
	Jojoba oil	1.7 parts by weight
	Methyl phenyl polysiloxane	1 part by weight
	Suprofen	1 part by weight
	4-n-Butylresorcinol	0.1 part by weight
(b)	1,3-Butanediol	8 parts by weight
	Alkyl acrylate/methacrylate copolymer (Pemrene TR-2)	0.2 part by weight
	Potassium hydroxide	0.1 part by weight
	Maltotriose	0.2 part by weight
	Water	86.4 parts by weight

[0073]

<Example 13>

A medicament 2 (milky lotion) for external application to the skin which was an emulsified composition of the present invention for antifungal use was manufactured according to the formulation as shown in the following Table 12. Thus, each of the components (a) and (b) was heated at 80°C, (b) was gradually added to (a) with stirring to emulsify and the mixture was treated with a homogenizer to homogenize the emulsified particles and then cooled to give an emulsified composition containing no nonionic surface-active agent. The resulting medicament 2 for external application to the skin showed a very good spread and gave little detachment from the skin whereby it was found to use a very good substrate material for medicaments.

. [0074]

When the above medicament 2 for external application to the skin was administered to the inflamed skin in the use of antifungal agent, the unfavorable physical irritation by the administration was ascertained to be suppressed. In addition, as a result of the antibacterial action of the resorcinol derivative, no deposition of dyes was noted in the skin after recovery from inflammation.

[0075]

Table 12

(a)	Jojoba alcohol	0.5 part by weight
	Cetanol	0.5 part by weight
	Glycerol α -monooleyl ether	0.3 part by weight
	Jojoba oil	1.7 parts by weight
	Methyl phenyl polysiloxane	1 part by weight
	Butyl paraben	0.1 part by weight
	Terbinafine	1 part by weight
	4-n-Butylresorcinol	0.1 part by weight
(b)	1,3-Butanediol	8 parts by weight
	Alkyl acrylate/methacrylate copolymer (Pemrene TR-2)	0.2 part by weight
	Potassium hydroxide	0.1 part by weight
	Maltotriose	0.2 part by weight
	Water	86.3 parts by weight

[0076]

[Advantages of the Invention]

In accordance with the present invention, it is now possible to provide an emulsified composition containing a resorcinol derivative such as cosmetics and medicaments for external application to the skin where the pharmaceutical effect of the resorcinol is enhanced and, at the same time, sufficient safety and stability of the preparation are ensured.

[End]